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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/577,897	05/24/2000	H. Robert Horvitz	01997/198007	5616

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EXAMINER
SHUKLA, RAM R

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 03/14/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/577,897	Applicant(s) HORVITZ ET AL.	
	Examiner Ram R. Shukla	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 6 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 6 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The application has been withdrawn from issue because of new art issues and other patentability issues. A new office action follows.

2. Claim 6 is pending.

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claim 6 is rejected under the judicially created doctrine of double patenting over claim 1 of U. S. Patent No. 5,962,301 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: The protein of claim 1 of the '301 patent (SEQ ID NO 2) has x at positions 27, 65, 360 and 449, whereas in the protein of claim 6 (SEQ ID NO 19) of the instant application, there is a particular amino acid at each of these positions. In fact the figure 3 of the '301 patent and figure 4 of the instant application are the same and disclose the same nucleic acid and amino acid sequence. The amino acid sequence of figure 4 of the instant application is the sequence of SEQ ID NO 19 of the instant application. Therefore,

the amino acid sequence of SEQ ID NO 19 of the instant application is disclosed in the '301 patent.

Furthermore, there is no apparent reason why applicant was prevented from presenting claims corresponding to those of the instant application during prosecution of the application, which matured into a patent. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 6 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 6 is drawn to the amino acid sequence of SEQ ID NO 19.
The specification as filed is not enabling for the claimed invention because the specification as filed does not teach how to make the claimed protein and how to use the claimed protein and an artisan of skill at the time of the invention would have required undue experimentation to make and use the protein, as discussed below.

While determining whether a specification is enabling, one considers whether the claimed invention provides sufficient guidance to make and use the claimed invention, if not, whether an artisan would have required undue experimentation to make and use the claimed invention and whether working examples have been provided. When determining whether a specification meets the enablement requirements, some of the factors that need to be analyzed are: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of

ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and whether the quantity of any necessary experimentation to make or use the invention based on the content of the disclosure is "undue" (In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). Furthermore, USPTO does not have laboratory facilities to test if an invention will function as claimed when working examples are not disclosed in the specification, therefore, enablement issues are raised and discussed based on the state of knowledge pertinent to an art at the time of the invention, therefore skepticism raised in the enablement rejections are those raised in the art by artisans of expertise.

The specification on page 58 discloses the characteristics of the Ced-3 protein that it is a serine rich protein and that it could be a target for kinases. Pages 11-12 of the specification further disclose the putative characteristics of the protein. The specification further teaches that ced-3 is responsible for programmed cell death. It is noted that nowhere in the specification, the method for producing the ced-3 protein has been described. A post filing art (Xue et al. Genes and Development 10:1073-2083, 1996) by the inventor's group showed that ced-3 is a cysteine protease and that the protein underwent self-proteolytic cleavage and therefore, a full-length wild type protein could not be produced. For example, Xue et al teach that when expressed in E.coli, western blot analysis of the cell lysate detected three bands of 32, 15 and 13 kD, all of which are smaller than the 56 kD full length Ced-3 protein. This shows that an artisan would not have been able to produce the full length Ced-3 of SEQ ID NO 19. The specification does not provide any guidance as to how would an artisan of skill would have produced a protease, which cleaved itself. While the art taught production of full-length protein by in vitro translation in a rabbit reticulocyte lysate, the specification does not teach such a method and there is no evidence of record that an artisan would have used such a method and even if one had used, how would an artisan have isolated and purified the protein from the lysate to get a full length active protein. Yet another post filing art similarly was not able to express and isolate the full length protein (see Wu et al. The Journal of Biological Chemistry 272:21449-21454, 1997). While the

investigators in this art used a mutant to produce a full length Ced-3 protein, the specification does not provide any teaching as to what modification in ced-3 sequence would have been required to produce the full-length protein. It is emphasized that these two post-filing arts cannot be used to support the specification because the methods used by none of these arts are disclosed in the specification.

Next the specification does not teach how to use the protein. While the specification has disclosed vaguely about using the protein, for example, on page 3, lines 13-18, the specification states " This invention further relates to methods for altering..... the activity of the cell death genes or their encoded products in cells....." or on page 7, in the section on detailed description of the invention, the specification states "The activity of a cell death gene is intended to include the activity of the gene itself and of the encoded products of the genes. Thus, agents.....include those which affects the expression as well as the function of the encoded RNA and protein....." or on page 19, in the section on testing of agents, the specification states "The activity of the agent can be verified both by in vivo bioassays.....and by in vitro systems, in which the genes are expressed in the cultured cells or in which the isolated or synthetic gene products are tested directly in biochemical experiments", the specification does not provide any specific teaching as to how to use the protein.

An artisan of skill would have required extensive experimentation to determine how to make and use the claimed invention and in view of unpredictability of producing a full length protein as evidence by the post filing art, an artisan would not have known what method to use for producing the protein and use it and therefore the experimentation would have been undue.

7. No claim is allowed.

When amending claims, applicants are advised to submit a clean version of each amended claim (without underlining and bracketing) according to § 1.121(c).

For instructions, Applicants are referred to http://www.uspto.gov/web/offices/dcom/olia/aipa/index.htm.

Applicants are also requested to submit a copy of all the pending/under consideration claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (703) 305-1677. The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for this Group is (703) 308-4242. Any inquiry of a general nature, formal matters or relating to the status of this application or proceeding should be directed to the William Phillips whose telephone number is (703) 305-3413.

Ram R. Shukla

RAM R. SHUKLA, PH.D
PATENT EXAMINER

Ram R. Shukla, Ph.D.
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